REMARKS

The Office Action

Claims 1-23 were pending and under examination as of the last Office Action. All claims stand rejected under 35 U.S.C § 112, second paragraph, and under 35 U.S.C. § 103(a). Applicants address each of the rejections below.

Amendments to the Specification

Applicants have amended the specification to capitalize the trademark names WELLFERON, ALFERON, SUMIFERON, MULIFERON, ROFERON-A, INTRON-A, BEROFOR ALPHA 2, and INFERGEN, as required by the Office. Applicants note that the generic terminology for these trademark names is found on page 4, lines 2-8, of the specification as filed.

Amendments to the Claims

Claims 1, 11, and 21 have been amended to recite a second anti-neoplastic therapy. Support for these amendments is found, for example, in claims 9 and 20 of the specification as filed, and on page 5, line 24 to page 6, line 2, of the specification as filed. Claims 9 and 20 have been canceled, and claim 10 has been amended to depend from claim 1. New claims 24 and 25 recite the limitations of claim 10, where a "second anti-neoplastic therapy is chemotherapy or radiation therapy," and depend from claims 11 and 21, respectively. Support for the addition of new claims 24 and 25 can be found, for example, in claim 10, and on page 5, lines 24, to page 6, line 2, of the specification as filed. Claim 14 has been amended to depend from claim 11 rather than from claim 13. Additionally, claims 14, 21, and 23 have been amended for purposes of clarity.

The present amendments were made solely to expedite prosecution, and applicants reserve the right to pursue any canceled subject matter in this or in a continuing application. No new matter has been added.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-23 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. According to the Office (page 2), the claims fail "to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The metes and bound of the term 'asialo-interferon' are not clear." Applicants disagree, and point out that the language of the claim, read in light of the specification, is sufficiently clear to meet the standard set by 35 U.S.C § 112, second paragraph.

In particular, applicants' specification clearly defines the term "asialo-interferon" (page 5, lines 5-23):

> By "asialo-interferon" is meant a glycosylated interferon lacking a terminal sialic group that is present in the native glycosylated interferon. Removal of the terminal sialic acid residue exposes the underlying galactose moiety. It is the terminal galactose that is recognized by the asialoglycoprotein receptor. Preferably, asialo-interferon contains at least 50%, 70%, 80%, 90%, or even 95% of the carbohydrate moieties present in the native interferon. Most preferably, asialo-interferon lacks only the terminal sialic acid residue. Asialo-interferons can be produced by removing one or more sialic acid groups from a glycosylated interferon, such as interferon-α, -β, or -γ. This removal may be accomplished, for example, by mild acid hydrolysis, or treatment of native glycosylated interferon, such as interferon-α, -β, or -γ, with purified neuroaminidase. For interferons containing more than one sugar chain, selective desialylation may be accomplished using specific neuroaminidase (sialidase) enzymes. Specifically excluded by this definition are completely deglycosylated interferons, including interferons that are typically produced by prokaryotic cells and interferons produced by eukaryotic cells and enzymatically or chemically deglycosylated. Of course, because the goal of removing the sialic acid residue is to create a glycosylated interferon having at least one terminal galactose residue on an oligosaccharide chain, a terminal galactose residue may be engineered by any other appropriate means including, for example, covalently attaching an oligosaccharide to a deglycosylated interferon.

Given this description, one skilled in the art would readily understand the meaning of the term "asialo-interferon" to mean a glycosylated interferon lacking a terminal sialic group, as defined on page 5, lines 10-11. The Office cites references (Marchal et al.,

Biol. Chem. (2001) 382:151-159; Altmann et al., *Glycoconjugate* (1999) 16:109-123; Sugyiami et al., *Eur. J. Biochem.* (1993) 217:921-927; Goochee et al., *Bio/Technology* (1991) 9:1347-1355; and Krezdorn et al., *Eur. J. Biochem.* (1994) 220:809-817) to show that not all native interferons are sialylated. However, one skilled in the art would understand the reference to "native glycosylated interferons" on page 5, line 6, to be purely illustrative. As such, this description "reasonably apprises those skilled in the art" of the scope of the present claims. See, for example, *Miles Laboratories, Inc. v. Shandon, Inc.*, 997 F.2d 870, 27 U.S.P.Q.2d 1123 (Fed. Cir. 1993) ("If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more...The degree of precision necessary for adequate claims is a function of the nature of the subject matter."). Accordingly, the rejection under 35 U.S.C. § 112, second paragraph, may be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Takahashi (U.S. Patent No. 6,296,844) in view of Trere et al. (*Br. J. Cancer* (1999) 81:404-408; "Trere") and Treiber (*Digestive Diseases* (2001) 19:311-323), as well as Takahashi in view of Kudo et al. (*J. Nuc. Med.* (1991) 32:1177-1182; "Kudo") and Treiber. For the reasons discussed below, the limited disclosure of each of these references is insufficient to motivate the skilled artisan to move away from the methods disclosed in each of these references to the presently claimed methods.

Claims 1, 11, and 21

Claims 1-13 and 15-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Takahashi in view of Trere and Treiber.

Takahashi does not teach or suggest the limitations of amended claims 1, 11, and 21, which requires administering asialo-IFN *in combination with a second anti-neoplastic therapy* (see, for example, page 3 (lines 3-5), page 5 (line 24) – page 6 (line 2), page 16

(line 15-18), and page 22 (line 16-20) of the specification as filed). Takahashi clearly guides the skilled artisan towards the use of asialo-IFN monotherapy. Takahashi does not motivate the skilled artisan to look beyond the discussed treatment modalities, much less to employ asialo-IFN combination therapies as presently claimed.

Trere or Treiber, alone or in combination, fail to remedy this deficiency. Trere does not teach or suggest administering an asialo-IFN to a patient having liver cancer. Trere also does not teach or suggest administering an asialo-IFN in combination with a second anti-neoplastic therapy. Treiber, like Trere, provides no motivation for the claimed method of treatment, especially given that Treiber, in connection with systemic treatment of hepatocellular carcinoma (HCC), explicitly states, at page 322, "except for patients with chronic viral hepatitis in whom IFN can effectively prevent HCC recurrence [citations omitted], no clear recommendation [for HCC therapy] can be made." In the absence of any reasoning to administer a combination asialo-IFN and anti-neoplastic therapy, there is no motivation to combine the cited references, and thus, in connection with the presently-claimed invention, there is no *prima facie* case of obviousness under 35 U.S.C. § 103(a).

Claim 14

Claim 14 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Takahashi in view of Kudo and Treiber.

As is discussed above, the combination of Takahashi and Treiber fails to teach, suggest, or provide motivation to combine asialo-IFN with a second anti-neoplastic therapy. Kudo, like Takahashi and Treiber, fails to teach or suggest use of both asialo-IFN and a second anti-neoplastic therapy. As Takahashi, Treiber, and Kudo, alone or in combination, fail to teach, suggest, or motivate the skilled worker to render the claimed invention obvious, this rejection may also be withdrawn.

CONCLUSION

Applicant submits that the claims are in condition for allowance and such action is respectfully requested. Enclosed is a petition to extend the period for replying for three months, to and including September 22, 2006.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 22-Sep-2006

James D. DeCamp, Ph.D.
Reg. No. 43,580

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045